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     FILE 'HCAPLUS' ENTERED AT 08:46:25 ON 30 JUN 2009
L1              STRUCTURE UPLOADED
                S L1

     FILE 'REGISTRY' ENTERED AT 08:46:45 ON 30 JUN 2009
L2            0 S L1

     FILE 'HCAPLUS' ENTERED AT 08:46:46 ON 30 JUN 2009
L3            0 S L2
                S L1

     FILE 'REGISTRY' ENTERED AT 08:47:36 ON 30 JUN 2009
L4            2 S L1 SSS FUL

     FILE 'HCAPLUS' ENTERED AT 08:47:37 ON 30 JUN 2009
L5            6 S L4 SSS FUL


     FILE 'HCAPLUS' ENTERED AT 08:48:14 ON 30 JUN 2009
L6            0 S L2
L7            6 S L4
L8        45137 S MYCOBACTERIUM OR MYCOBACTERIAL
L9        10039 S (GLUTAMYLCYSTEINE OR GLUTAMINE OR GLUTATHIONE)(W)SYNTHETASE
L10          96 S L8 AND L9
L11          45 S L10 AND (PY<2003 OR AY<2003 OR PRY<2003)
L12     1410944 S INHIBITION OR INHIBITING OR INHIBITED OR INACTIVATED
L13          10 S L11 AND L12
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=> file hcaplus
COST IN U.S. DOLLARS | SINCE FILE ENTRY | TOTAL SESSION
FULL ESTIMATED COST | 0.22 | 0.22

FILE 'HCAPLUS' ENTERED AT 08:46:25 ON 30 JUN 2009
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FILE COVERS 1907 - 30 Jun 2009 VOL 151 ISS 1
FILE LAST UPDATED: 29 Jun 2009 (20090629/ED)
REVISED CLASS FIELDS (/NCL) LAST RELOADED: Apr 2009
USPTO MANUAL OF CLASSIFICATIONS THESAURUS ISSUE DATE: Apr 2009

HCAplus now includes complete International Patent Classification (IPC)
reclassification data for the second quarter of 2009.

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http://www.cas.org/legal/infopolicy.html

This file contains CAS Registry Numbers for easy and accurate
substance identification.

=>
Uploading C:\Program Files\STNEXP\Queries\10534660verify.str

chain nodes :
1 2 3 4 5 6 7 8 9 10
chain bonds :
1-2 2-3 2-9 2-10 3-4 4-5 5-6 5-7 5-8
exact/norm bonds :
2-9 2-10 5-7 5-8

exact bonds :
1-2 2-3 3-4 4-5 5-6

Connectivity :
10:1 E exact RC ring/chain
Match level :
1:CLASS 2:CLASS 3:CLASS 4:CLASS 5:CLASS 6:CLASS 7:CLASS 8:CLASS 9:CLASS
10:CLASS
Generic attributes :
10:
Saturation   : Saturated

Element Count :
Node 10: Limited
    C,C1-8

L1   STRUCTURE UPLOADED

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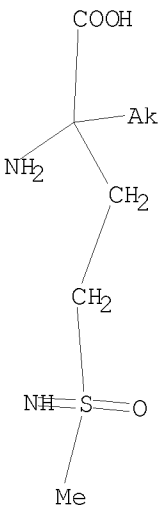
L1   STR



Structure attributes must be viewed using STN Express query preparation.

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L2 NOT FOUND
The L-number entered has not been defined in this session, or it
has been deleted. To see the L-numbers currently defined in this
session, enter DISPLAY HISTORY at an arrow prompt (=>).

=> s l1
   REG1stRY INITIATED
Substance data SEARCH and crossover from CAS REGISTRY in progress...

Use DISPLAY HITSTR (or FHITSTR) to directly view retrieved structures.

SAMPLE SEARCH INITIATED 08:46:45 FILE 'REGISTRY'
SAMPLE SCREEN SEARCH COMPLETED - 12 TO ITERATE

100.0% PROCESSED 12 ITERATIONS 0 ANSWERS
SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS: ONLINE **COMPLETE**
BATCH **COMPLETE**
PROJECTED ITERATIONS: 33 TO 447
PROJECTED ANSWERS: 0 TO 0

L2 0 SEA SSS SAM L1

L3 0 L2

=> s l1 sss ful
REG1stRY INITIATED
Substance data SEARCH and crossover from CAS REGISTRY in progress...
Use DISPLAY HITSTR (or FHITSTR) to directly view retrieved structures.

FULL SEARCH INITIATED 08:47:37 FILE 'REGISTRY'
FULL SCREEN SEARCH COMPLETED - 174 TO ITERATE

100.0% PROCESSED 174 ITERATIONS 2 ANSWERS
SEARCH TIME: 00.00.01

L4 2 SEA SSS FUL L1

L5 6 L4

=> d l5 scan

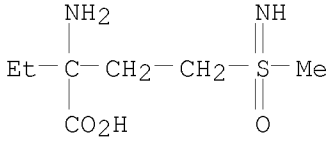
L5 6 ANSWERS HCAPLUS COPYRIGHT 2009 ACS on STN
CC 3-5 (Biochemical Interactions)
Section cross-reference(s): 7
TI Inhibition of glutathione biosynthesis by prothionine sulfoximine (S-n-propyl homocysteine sulfoximine), a selective inhibitor of γ-glutamylcysteine synthetase
ST glutathione formation prothionine sulfoximine; glutamylcysteine synthetase prothionine sulfoximine
IT Kidney, metabolism
(glutathione formation by, prothionine sulfoximine inhibition of)
IT Molecular structure-biological activity relationship
(glutamylcysteine synthetase-inhibiting, of prothionine sulfoximine analogs)
IT 70-18-8, biological studies
RL: FORM (Formation, nonpreparative)

(formation of, by kidney, methionine sulfoximine inhibition of)
IT 15985-39-4 66735-67-9 66735-68-0
RL: PRP (Properties)
(glutamylcysteine synthetase inhibition by)
IT 9023-64-7
RL: PROC (Process)
(methionine sulfoximine inhibition of)
IT 15985-39-4P 70056-00-7P 70056-01-8P 70056-02-9P 70056-03-0P
70056-05-2P 70085-86-8P 70085-87-9P
RL: PREP (Preparation)
(preparation and glutamylcysteine synthetase-inhibiting activity of)
IT 44768-66-3P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation and hydantoinylation of)
IT 70085-85-7P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and saponification of)
IT 557-02-8P 2598-46-1P 2749-07-7P 16820-52-3P 16820-66-9P
42537-72-4P 70056-04-1P 70056-06-3P 70095-14-6P
RL: PREP (Preparation)
(preparation of)
IT 9023-70-5
RL: PRP (Properties)
(prothionine sulfoximine inhibition of glutamylcysteine synthetase in relation to)
IT 107-03-9
RL: RCT (Reactant); RACT (Reactant or reagent)
(reaction of, with acrolein)
IT 107-02-8, biological studies
RL: RCT (Reactant); RACT (Reactant or reagent)
(reaction of, with propanethiol)
IT 14109-74-1
RL: RCT (Reactant); RACT (Reactant or reagent)
(reductive amination of)

HOW MANY MORE ANSWERS DO YOU WISH TO SCAN? (1):0

=> d l4 scan
YOU HAVE REQUESTED DATA FROM FILE 'REGISTRY' - CONTINUE? (Y)/N:y

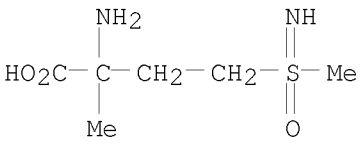
L4 2 ANSWERS REGISTRY COPYRIGHT 2009 ACS on STN
IN Butanoic acid, 2-amino-2-ethyl-4-(S-methylsulfonimidoyl)- (9CI)
MF C7 H16 N2 O3 S



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

HOW MANY MORE ANSWERS DO YOU WISH TO SCAN? (1):1

L4 2 ANSWERS REGISTRY COPYRIGHT 2009 ACS on STN
IN Isovaline, 4-(S-methylsulfonimidoyl)- (9CI)
MF C6 H14 N2 O3 S



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

ALL ANSWERS HAVE BEEN SCANNED

=> file hcaplus
COST IN U.S. DOLLARS SINCE FILE ENTRY TOTAL SESSION
FULL ESTIMATED COST 2.85 198.46

FILE 'HCAPLUS' ENTERED AT 08:48:14 ON 30 JUN 2009
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FILE COVERS 1907 - 30 Jun 2009 VOL 151 ISS 1
FILE LAST UPDATED: 29 Jun 2009 (20090629/ED)
REVISED CLASS FIELDS (/NCL) LAST RELOADED: Apr 2009
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This file contains CAS Registry Numbers for easy and accurate substance identification.

=> s l2
L6 0 L2

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=> s l4
L7           6 L4

=> d l7 1-6 ti abs bib hitstr

L7   ANSWER 1 OF 6  HCAPLUS  COPYRIGHT 2009 ACS on STN
TI   Anti-microbial agents derived from methionine sulfoximine analogues and
     use for treating mycobacterial infections
AB   Novel antimicrobial compns. containing analogs of L-methionine-SR-sulfoximine
     (MSO) that are effective in treating intracellular pathogen infections are
     provided.  Specifically, the compns. provided are MSO analogs having
     superior antimicrobial activity with significantly less toxicity as
     compared to MSO.  These MSO analogs are suitable for use in treating
     infection in animals including primates, cows, pigs, horses, rabbits,
     mice, rats, cats, and dogs.  Moreover, the MSO analogs are ideally suited
     for treating infections caused by the genus Mycobacterium.  Addnl.,
     methods for using the novel MSO analogs are also provided.
AN   2004:452975  HCAPLUS <<LOGINID::20090630>>
DN   141:12262
TI   Anti-microbial agents derived from methionine sulfoximine analogues and
     use for treating mycobacterial infections
IN   Harth, Gunter; Griffith, Owen W.; Horwitz, Marcus A.
PA   Regents of the University of California, USA
SO   PCT Int. Appl., 40 pp.
     CODEN: PIXXD2
DT   Patent
LA   English
FAN.CNT 1
     PATENT NO.          KIND   DATE        APPLICATION NO.        DATE
     ---------------     ----   --------    --------------------   --------
PI   WO 2004045539        A2    20040603    WO 2003-US36705        20031117
     WO 2004045539        A9    20040805
     WO 2004045539        A3    20041111
         W:  AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,
             CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH,
             GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR,
             LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH,
             PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ,
             UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
         RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE,
             IT, LU, MC, NL, PT, RO, SE, SI, SK, TR
     AU 2003295579        A1    20040615    AU 2003-295579         20031117
     US 20040157802       A1    20040812    US 2003-715679         20031117
     US 20060142251       A1    20060629    US 2005-534660         20051128
PRAI US 2002-426502P      P     20021115
     US 2002-430407P      P     20021202
     WO 2003-US36705      W     20031117
OS   MARPAT 141:12262
IT   66735-67-9 66735-68-0
     RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
        (anti-microbial agents derived from methionine sulfoximine analogs and
        use for treating mycobacterial infections)
RN   66735-67-9  HCAPLUS
CN   Isovaline, 4-(S-methylsulfonimidoyl)- (9CI)  (CA INDEX NAME)
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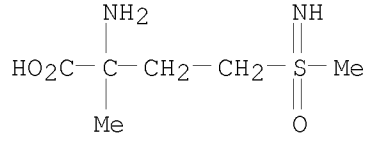
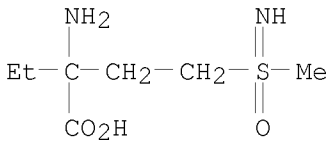


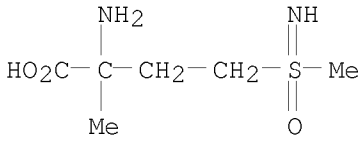
RN 66735-68-0 HCAPLUS
CN Butanoic acid, 2-amino-2-ethyl-4-(S-methylsulfonimidoyl)- (9CI) (CA INDEX NAME)



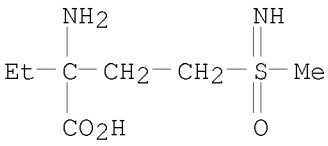
L7 ANSWER 2 OF 6 HCAPLUS COPYRIGHT 2009 ACS on STN
TI Pyruvate analog adducts with NAD as lactate dehydrogenase inhibitors
AB Adducts of pyruvate and NAD+ adducts are lactate dehydrogenase inhibitors that can pass through the blood-brain barrier and are of use in the treatment of primary systemic lactic acidosis are prepared and characterized. A series of Na arylidene pyruvates were prepared and the adducts with NAD+ prepared by standard chemical These were then tested for inhibition of beef heart and rat brain lactate dehydrogenases. An NAD-pyruvate reduced the activity of the beef heart enzyme to 90% of control values and reduced the activity of the rat brain enzyme to 48% of controls in the presence of 0.24 mM pyruvate. An aldehyde analog was similarly active in the nanomolar range. Inhibition of lactate dehydrogenase activity in synaptosomes was also demonstrated.
AN 1991:38443 HCAPLUS <<LOGINID::20090630>>
DN 114:38443
OREF 114:6623a,6626a
TI Pyruvate analog adducts with NAD as lactate dehydrogenase inhibitors
IN Cooper, Arthur J. L.
PA Cornell Research Foundation, Inc., USA
SO U.S., 8 pp.
CODEN: USXXAM
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI US 4950602	A	19900821	US 1987-16894	19870220
PRAI US 1987-16894		19870220		

OS MARPAT 114:38443
IT 66735-67-9
RL: BIOL (Biological study)
(oxopentenoate from, reaction with NAD of, in preparation of lactate dehydrogenase inhibitor capable of passing blood-brain barrier, preparation of)
RN 66735-67-9 HCAPLUS
CN Isovaline, 4-(S-methylsulfonimidoyl)- (9CI) (CA INDEX NAME)

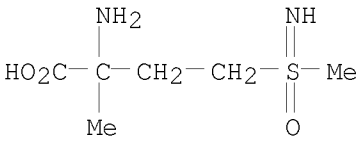


L7 ANSWER 3 OF 6 HCAPLUS COPYRIGHT 2009 ACS on STN
TI Amino acid sulfoximines: α-ethylmethionine sulfoximine
AB α-Ethylmethionine sulfoxime, HO2CCEt(NH2)CH2CH2S(O)Me:NH, was prepared by treatment of HO2CCEt(NH2)CH2CH2SMe (I) with HCl. I was prepared by treatment of EtCOCH:CH2 with MeSH to give EtCOCH2CH2SMe which was converted to a hydantoin derivative with (NH4)2CO3 and NaCN and the product hydrolyzed to I.
AN 1988:132274 HCAPLUS <<LOGINID::20090630>>
DN 108:132274
OREF 108:21719a,21722a
TI Amino acid sulfoximines: α-ethylmethionine sulfoximine
AU Griffith, Owen W.
CS Med. Coll., Cornell Univ., New York, NY, 10021, USA
SO Methods in Enzymology (1987), 143(Sulfur Sulfur Amino Acids), 286-91
CODEN: MENZAU; ISSN: 0076-6879
DT Journal
LA English
IT 66735-68-0P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)
RN 66735-68-0 HCAPLUS
CN Butanoic acid, 2-amino-2-ethyl-4-(S-methylsulfonimidoyl)- (9CI) (CA INDEX NAME)

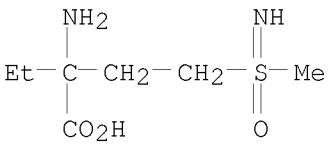


L7 ANSWER 4 OF 6 HCAPLUS COPYRIGHT 2009 ACS on STN
TI Inhibition of glutathione biosynthesis by prothionine sulfoximine (S-n-propyl homocysteine sulfoximine), a selective inhibitor of γ-glutamylcysteine synthetase
AB DL-Prothionine SR-sulfoximine [70085-86-8] and α-methyl-DL-prothionine-SR-sulfoximine [70056-05-2] were prepared and found to markedly inhibit γ-glutamylcysteine synthetase [9023-64-7] but to not significantly affect glutamine synthetase [9023-70-5]. After injection of prothionine sulfoximine into mice, the level of kidney glutathione [70-18-8] decreased rapidly to .apprx.20% of the control level indicating that a large fraction, rather than a small pool, of glutathione participates in rapid turnover. The rapid decline of the glutathione level that occurs after inhibition of glutathione synthesis reflects the normal rate of intracellular glutathione utilization by the γ-glutamyl cycle. A number of related sulfoximines were synthesized and tested as inhibitors of glutamine and γ-glutamylcysteine synthetases.
AN 1979:198299 HCAPLUS <<LOGINID::20090630>>
DN 90:198299
OREF 90:31455a,31458a
TI Inhibition of glutathione biosynthesis by prothionine sulfoximine (S-n-propyl homocysteine sulfoximine), a selective inhibitor of γ-glutamylcysteine synthetase
AU Griffith, Owen W.; Anderson, Mary E.; Meister, Alton
CS Med. Coll., Cornell Univ., New York, NY, USA
SO Journal of Biological Chemistry (1979), 254(4), 1205-10

CODEN: JBCHA3; ISSN: 0021-9258
DT Journal
LA English
IT 66735-67-9 66735-68-0
RL: PRP (Properties)
(glutamylcysteine synthetase inhibition by)
RN 66735-67-9 HCAPLUS
CN Isovaline, 4-(S-methylsulfonimidoyl)- (9CI) (CA INDEX NAME)

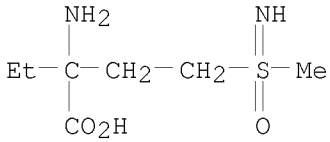


RN 66735-68-0 HCAPLUS
CN Butanoic acid, 2-amino-2-ethyl-4-(S-methylsulfonimidoyl)- (9CI) (CA INDEX NAME)

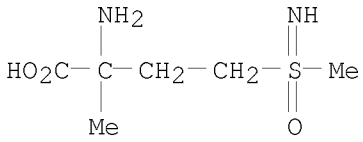


L7 ANSWER 5 OF 6 HCAPLUS COPYRIGHT 2009 ACS on STN
TI Differential inhibition of glutamine and γ-glutamylcysteine synthetases by α-alkyl analogs of methionine sulfoximine that induce convulsions
AB α-Methyl-DL-methionine (SR)-sulfoximine [66735-67-9] and α-ethyl-DL-methionine (SR)-sulfoximine [66735-68-0], like L-methionine (SR)-sulfoximine [15985-39-4], induced convulsions in mice and inhibited glutamine synthetase [9023-70-5] irreversibly; α-ethylmethionine sulfoximine was .apprx.50% as inhibitory as methionine sulfoximine and α-methylmethionine sulfoximine. However, whereas α-methylmethionine sulfoximine and methionine sulfoximine inhibited γ-glutamylcysteine synthetase [9023-64-7] markedly, α-ethylmethionine sulfoximine did not, nor did administration of the α-Et analog produce the decrease in tissue glutathione [70-18-8] levels found after giving methionine sulfoximine or its α-Me analog. The α-alkyl methionine sulfoximine analogs cannot be catabolized via the corresponding α-keto or α-imino acids, and, like other α-substituted amino acids, are probably not metabolized to a significant extent in vivo; this suggests that the amino acid sulfoximine mols. themselves, rather than their metabolites, are directly involved in the induction of convulsions. Possible explanations for the reported lack of correlation between the occurrence of convulsions and the levels of glutamine synthetase activity (and its substrates and product) are considered.
AN 1978:500916 HCAPLUS <<LOGINID::20090630>>
DN 89:100916
OREF 89:15375a,15378a
TI Differential inhibition of glutamine and γ-glutamylcysteine synthetases by α-alkyl analogs of methionine sulfoximine that induce

convulsions
AU Griffith, Owen W.; Meister, Alton
CS Dep. Biochem., Cornell Univ. Med. Coll., New York, NY, USA
SO Journal of Biological Chemistry (1978), 253(7), 2333-8
CODEN: JBCHA3; ISSN: 0021-9258
DT Journal
LA English
IT 66735-68-0
RL: PRP (Properties)
(glutamine synthetase and glutamylcysteine synthetase inhibition by, convulsions in relation to)
RN 66735-68-0 HCAPLUS
CN Butanoic acid, 2-amino-2-ethyl-4-(S-methylsulfonimidoyl)- (9CI) (CA INDEX NAME)



IT 66735-67-9P
RL: PREP (Preparation)
(preparation and glutamine synthetase and glutamylcysteine synthetase inhibition by)
RN 66735-67-9 HCAPLUS
CN Isovaline, 4-(S-methylsulfonimidoyl)- (9CI) (CA INDEX NAME)



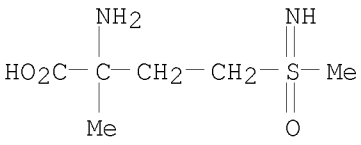
L7 ANSWER 6 OF 6 HCAPLUS COPYRIGHT 2009 ACS on STN
TI Sulfur-containing amino acids
GI For diagram(s), see printed CA Issue.
AB MeCH:CHCHO (140 g.) and 96 g. MeSH in the presence of 2 drops of piperidine stirred 0.5 hr. at 5-10° and 3 hrs. at room temperature, the mixture treated with an addnl. 28 g. MeSH, heated about 1 hr. at 90°, diluted with 500 cc. Et2O, washed with dilute HCl and H2O, dried, and evaporated, and the residue distilled gave 201 g. MeSCHMeCH2CHO (I), b23 80°. AcCH:CH2 (27 g.) and 18 g. MeSH yielded 35.4 g. Ac(CH2)2SMe, b55 106°, nD25 1.4711. I (48.5 g.), 113 g. (NH4)3SO3, 25.5 g. NaCN, 335 cc. EtOH, and 335 cc. H2O heated 5 hrs. with stirring at 55°, the mixture concentrated to about 300 cc., treated cautiously with 50 cc. concentrated HCl, heated 7 min. at about 90°, refrigerated, and filtered, and the residue washed with 200 cc. H2O yielded 49 g. 5-(β-benzylmercapto)propylhydantoin, m. 117-18°(from EtOAc). Similarly were prepared the following compds. RR'C.CO.NH.CO.NH (R, R', m.p., and % yield given): MeS(CH2)2, Me, 109.5-10.5°, 93.8; MeSCHMeCH2, H, 191-2°, 50.1; MeSCHPhCH2, H, 173-4°, 491.

S-Benzyl-4-methylhomocysteine (7.17 g.), m. 222.5-3.5° (decomposition) (from H2O) (obtained in 94% yield from the hydantoin) (0.69,0.74, 0.93) (the figures given in parentheses through out this abstract represent the Rf values of the resp. compds. obtained by ascending paper chromatography with BuOH-AcOH, lutidine-collidine, and PhOH-H2O, resp.) in 300 cc. liquid NH3 treated with about 1.7 g. Na, the solution decolorized with about 1 g. NH4Cl, treated with 5 cc. MeI, and evaporated, the residue treated with 125 cc. H2O, washed with Et2O, filtered, neutralized with concentrated HCl to pH about 6, concentrated to about 50 cc., diluted with 50 cc. Me2CO, and refrigerated, and the crystalline deposit recrystd. from aqueous MeOH yielded 4.1 g. MeSCHMeCH2CH(NH2)CO2H (II), m. 236-7° (decomposition), (0.44, 0.53, 0.79). Similarly were prepared: MeS(CH2)2CMe(NH2)CO2H, 61%, m. 284-5° (decomposition) (from aqueous MeOH), (0.45, 0.50, 0.77); MeSCHPh(CH2)2CH(NH2)CO2H, 49.3%, m. 201-2° (decomposition) (from H2O). BzCH2SMe (21.8 g.) in 50 cc. dry Et2O added with stirring to 1.4 g. LiAlH4 in 10 cc. dry Et2O, the mixture refluxed 1 hr. with stirring, cooled, and treated with stirring with 200 cc. ice water and 100 cc. 5N H2SO4, the aqueous layer washed with Et2O, the combined Et2O solns. washed, dried, and evaporated under a jet of dry air, and the residue distilled gave 18.4 g. MeSCH2CH(OH)Ph (III), b1.8 113-14.5°. III (170 mg.) treated with MeI yielded III. MeI, m. 134-5° (decomposition). III (15.8 g.) in 25 cc. dry CHCl3 treated with cooling with 9.2 g. SOCl2 in 15 cc. dry CHCl3, the mixture cooled 0.5 hr., kept at room temperature overnight and evaporated, the residue heated gently with 5 cc. dry CHCl3 and 5 cc. SOCl2, and the mixture distilled gave 14.3 g. MeSCH2CHClPh (IV), b2.8 106-7°, nD25 1.5692. AcNHCH(CO2Et)2 (11.6 g.) and 200 mg. KI added with stirring to 1.23 g. Na in 100 cc. absolute EtOH, the mixture treated with 10 g. IV in 1 portion, stirred 2 hrs. at room temperature, refluxed 5 hrs., and filtered hot, the residue washed with about 50 cc. hot EtOH, the combined alc. solns. evaporated to dryness in vacuo, the residual oil kept at room temperature overnight, and the crystalline material washed with dilute HCl and H2O and dried in vacuo over KOH pellets yielded 16 g. MeSCH2CHPhC(NHAc)(CO2Et)2 (V), m. 95-6° (from Et2O-pentane). Crude V (14.4 g.), 40 cc. H2O, and 10 cc. concentrated HCl refluxed 6 hrs. with stirring, the mixture treated with 40 cc. H2O and 10 cc. concentrated HCl, refluxed 1.5 hrs. with stirring, cooled to room temperature, the solid refluxed 8 hrs. with stirring with 80 cc. glacial AcOH and 10 cc. concentrated HCl, treated with Norit, and filtered, the residue washed with H2O, the combined filtrates evaporated in vacuo, the residue (about 10 g.) triturated with 50 cc. Me2CO and filtered, and the residue washed with Me2CO and dried yielded 5 g. MeSCH2CHPhCH(NH2)CO2H.HCl (VI.HCl), m. 208-9° (decomposition); the Me2CO solns. combined and evaporated to dryness, the residue refluxed 6.5 hrs. with 25 cc. H2O, 25 cc. glacial AcOH, and 10 cc. concentrated HCl, the solution evaporated to dryness in vacuo, the residue washed with Me2CO and neutralized with AmNH2, and a 1-g. portion dissolved in 8 cc. H2O and neutralized with AmNH2 to pH 6, diluted with 25 cc. Me2CO, and filtered, and the residue washed with 15 cc. Me2CO yielded 300 mg. VI; the filtrate diluted with Me2CO gave a 2nd crop, 350 mg. MeSH (14 g.) passed with stirring and cooling into 1.2 g. Na in 150 cc. absolute MeOH, the mixture treated with stirring and cooling with 50 g. Me α-benzamidosenecioate, diluted with 200 cc. absolute MeOH and 200 cc. dry C6H6, stirred 1 hr. at room temperature, allowed to stand overnight, treated with 3.12 g. glacial AcOH, and evaporated to dryness in vacuo at room temperature, the residue washed with warm dry C6H6, the C6H6 evaporated, the residue (58 g.), 300 cc. 85% HCO2H, 300 cc. concentrated HCl, and 300 cc. H2O refluxed 6 hrs., the solution concentrated to about 50 cc., washed with Et2O, neutralized with

AmNH2 to pH 6, diluted with 350 cc. Me2CO, and refrigerated 2 days, and the white crystals washed with 300 cc. Me2CO and 200 cc. Et2O yielded 16.8 g. S-methylpenicillamine, m. 281-2° (0.38, 0.50, 0.80); it was also obtained in the same manner from 2-phenyl-4-isopropylidene-5-oxazolone and 30 g. MeSH. MeSH (16 g.) passed into 1.2 g. Na in 300 cc. absolute MeOH, the solution treated with cooling and stirring with 62.3 g. 2-phenyl-4-benzal-5-oxazolone in 500 cc. warm, dry C6H6, the mixture stirred about 1 hr., kept at room temperature, treated with 3.12 g. glacial AcOH, and evaporated to dryness in vacuo, the residue treated with 100 cc. warm C6H6 and filtered, the filtrate diluted with 100 cc. warm C6H6 and 500 cc. pentane, and chilled, and the deposit washed with 150 cc. pentane yielded 74 g. PhCH(SMe)CH(NHBz)CO2Me (VII), m. 97-8.5° (from EtOAc-pentane). Crude VII (32.9 g.) hydrolyzed with 150 cc. H2O, 150 cc. concentrated HCl, and 150 cc. 90% HCO2H, the solution concentrated in vacuo to near dryness, and the precipitate washed with three 100-cc. portions H2O, dissolved in 75 cc. H2O, neutralized to pH 6 with AmNH2, and chilled yielded 12.5 g. S-methyl-3-phenylcysteine, m. 178-9° (decomposition) (0.51, 0.65, 0.88). The following sulfoxides were prepared by oxidation of the appropriate sulfides with H2O2 by the method of Toennies and Kolb (C.A. 33, 5359.9) (% yield, m.p., and Rf values given): PhCH2S(O)CHMeCH2CH(NH2)CO2H, 64.7, 214-15° (decomposition) (from H2O), (0.45, 0.60, 0.92); MeS(O)CH2CH2CMe(NH2)CO2H, 91.8, 239.5-40.5° (decomposition) (from aqueous MeOH), (0.14, 0.35, 0.77); MeS(O)CHMeCH2CH(NH2)CO2H (VIII), 84.4, 213.5-14.5° (from aqueous MeOH), (0.13, 0.40, 0.80); MeS(O)CH2CHPhCH(NH2)CO2H, 74.4, 205-6° (decomposition) (from aqueous MeOH), (0.33, 0.59, 0.87); MeS(O)CHPhCH2CH(NH2)CO2H, 87.7, 189-90° (decomposition) (from aqueous MeOH), (0.33, 0.47, 0.85); Me2CHCH[S(O)Me]CH(NH2)CO2H, 77.7, 166-7° (from aqueous MeOH), (0.14, 0.40, 0.76); PhCH[S(O)Me]CH(NH2)CO2H, 73.2, 147-8° (decomposition) (from aqueous MeOH), (0.29, 0.54, 0.82). VIII (600 mg.), 3 cc. H2O, 2 cc. MeOH, 0.2 cc. concentrated HCl, and 2 cc. 30% H2O2 refluxed 2 hrs., treated with 1 cc. 30% H2O2, refluxed again 2 hrs., neutralized with AmNH2 to pH 6.5, diluted with 100 cc. Me2CO and filtered, and the residue washed with 50 cc. Me2CO yielded 550 mg. MeS(O2)CHMeCH2CH(NH2)CO2H, m. 230-1° (decomposition) (from aqueous MeOH), (0.14, 0.50, 0.72). In the same manner was prepared PhCH2S(O2)CH2CH2CH(NH2)CO2H, 70.6%, m. 229-30° (decomposition) (from H2O), (0.50, 0.65, 0.84). The following sulfones were prepared by the oxidation on the appropriate sulfides with H2O2 in the presence of NH4 molybdate and HClO4 by the method of Toennies and Kolb (C.A. 35, 6571.1) (% yield, m.p., and Rf values given): MeS(O2)CH2CH2CMe(NH2)CO2H, 73.6, 288-9° (decomposition) (from aqueous MeOH), (0.16, 0.45, 0.65); MeS(O2)CH2CHPhCH(NH2)CO2H (IX), 50.8, 222-3° (decomposition) (from H2O), (0.32, 0.61, 0.79); MeS(O2)CHPhCH2CH(NH2)CO2H (X), 95.4, 196.5-7.5° (decomposition), (0.37, 0.55, 0.79); Me2CHCH[S(O2)Me]CH(NH2)CO2H, 77.7, 166-7° (from aqueous MeOH), (0.14, 0.53, 0.68); MeS(O2)CHPhCH(NH2)CO2H, 51.2, 141-2°(decomposition) (from aqueous MeOH), (0.30, 0.52, 0.70). VIII (6.0 g.) treated dropwise with stirring at 3° with 10.4 cc. concentrated H2SO4, the mixture heated with stirring to 45°, treated during 1 hr. at 48° with 54 cc. 1.4N HN3 in CHCl3, then heated with stirring 5 hrs. at 48°, treated with 13.5 cc. HN3 solution, heated 5 hrs. with stirring at 50°, stirred overnight at room temperature, poured with stirring onto 75 g. crushed ice, neutralized with solid Ba(OH)2 to about pH 2.5 then to pH 5 with solid BaCO3, and centrifuged, the supernatant decanted, the residue mixed with H2O, centrifuged, and decanted, this operation repeated until free of amino acid, the combined aqueous solns. concentrated in vacuo at 50° to about 100 cc., treated with C, and filtered, and the filtrate concentrated to about 40 cc., filtered, and evaporated to dryness yielded 6.4 g. MeS(:NH)CHMeCH2CH(NH2)CO2H, m. 199-200°

(decomposition) (from aqueous MeOH), (0.08, 0.38, 0.71). In the same manner was
prepared: MeS(:NH)CH2CH2CHMe(NH2)CO2H,100, 199-200° (decomposition) (from aqueous MeOH), (0.10, 0.35, 0.67). IX (100 mg.) treated with about 60 mg. N-bromosuccinimide gave MeS(O2)CH2CHPhCHO, isolated as the 2,4-dinitrophenylhydrazone, m. 188-9° (decomposition). X gave similarly MeS(O2)CHPhCH2CHO, isolated as the 2,4-dinitrophenylhydrazone, decomposed at 196-8° with a change from yellow to red at 169°. Only 4 of the amino acids suppressed the multiplication of T2 bacteriophage of Escherichia coli strain A.T.C.C. number 11303 at pH 7 and 37° at 100 p.p.m. or less.

AN 1956:73727 HCAPLUS <<LOGINID::20090630>>
DN 50:73727
OREF 50:13802g-i,13803a-i,13804a-g
TI Sulfur-containing amino acids
AU Reisner, David B.
CS Wallace & Tiernan, Inc., Newark, NJ
SO Journal of the American Chemical Society (1956), 78, 2132-5
CODEN: JACSAT; ISSN: 0002-7863
DT Journal
LA Unavailable
OS CASREACT 50:73727
IT 66735-67-9P, Sulfoximine, 3-amino-3-carboxybutyl methyl
RL: PREP (Preparation)
(preparation of)
RN 66735-67-9 HCAPLUS
CN Isovaline, 4-(S-methylsulfonimidoyl)- (9CI) (CA INDEX NAME)



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S L1

FILE 'REGISTRY' ENTERED AT 08:46:45 ON 30 JUN 2009
L2 0 S L1

FILE 'HCAPLUS' ENTERED AT 08:46:46 ON 30 JUN 2009
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S L1

FILE 'REGISTRY' ENTERED AT 08:47:36 ON 30 JUN 2009
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L5 6 S L4 SSS FUL

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L7             6 S L4

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FULL ESTIMATED COST                                      36.69     235.15

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)          SINCE FILE      TOTAL
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CA SUBSCRIBER PRICE                                      -4.92      -4.92

 SESSION WILL BE HELD FOR 120 MINUTES
STN INTERNATIONAL SESSION SUSPENDED AT 08:48:42 ON 30 JUN 2009

Connecting via Winsock to STN



Welcome to STN International!  Enter x:X

LOGINID:SSPTAEXO1623

PASSWORD:
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DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)          SINCE FILE      TOTAL
                                                         ENTRY    SESSION
CA SUBSCRIBER PRICE                                      -4.92      -4.92

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          8023 MYCOBACTERIAL
L8       45137 MYCOBACTERIUM OR MYCOBACTERIAL

=> s (glutamylcysteine or glutamine or glutathione) synthetase
MISSING OPERATOR TATHIONE) SYNTHETASE
The search profile that was entered contains terms or
nested terms that are not separated by a logical operator.

=> s (glutamylcysteine or glutamine or glutathione)(w)synthetase
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         55095 GLUTAMINE
        108419 GLUTATHIONE
         54698 SYNTHETASE
L9       10039 (GLUTAMYLCYSTEINE OR GLUTAMINE OR GLUTATHIONE)(W)SYNTHETASE

=> s l8 and l9
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       4508023 AY<2003
       3977562 PRY<2003
L11         45 L10 AND (PY<2003 OR AY<2003 OR PRY<2003)

=> s inhibition or inhibiting or inhibited or inactivated
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        208599 INHIBITING
        635642 INHIBITED
         56184 INACTIVATED
L12    1410944 INHIBITION OR INHIBITING OR INHIBITED OR INACTIVATED

=> s l11 and l12
L13         10 L11 AND L12

=> d l13 1-10 ti abs bib

L13  ANSWER 1 OF 10  HCAPLUS  COPYRIGHT 2009 ACS on STN
TI   Use of antisense oligonucleotides to glutamine
     synthetase, aroA, ask, groES and antigen 85 complex genes of
     Mycobacterium tuberculosis in treatment of infections
AB   Methods of inhibiting the proliferation of Mycobacterium
     tuberculosis comprising contacting Mycobacterium tuberculosis
     with an effective amount of a polynucleotide complementary to an mRNA
     transcript expressed by Mycobacterium tuberculosis are provided.
     Typical methods of the invention utilize phosphorothioate modified
     antisense polynucleotides (PS-ODNs) against the mRNA of M.tuberculosis
     genes such as glutamine synthetase, aroA, ask, groES,
     and the genes of the Antigen 85 complex.  Optionally, the methods employ
     multiple antisense polynucleotides targeting different
     Mycobacterium tuberculosis transcripts.  In preferred embodiments
     of the invention, the antisense polynucleotides are complementary to the
     5' regions of the Mycobacterium tuberculosis transcripts.
AN   2002:906259  HCAPLUS <<LOGINID::20090630>>
DN   138:2188
TI   Use of antisense oligonucleotides to glutamine
     synthetase, aroA, ask, groES and antigen 85 complex genes of
     Mycobacterium tuberculosis in treatment of infections
IN   Horwitz, Marcus A.; Harth, Gunter; Zamecnik, Paul C.; Tabatadze, David
PA   The Regents of the University of California, USA
SO   PCT Int. Appl., 113 pp.
     CODEN: PIXXD2
DT   Patent
LA   English
FAN.CNT 2
     PATENT NO.          KIND   DATE        APPLICATION NO.        DATE
     ---------------     ----   --------    --------------------   --------
PI   WO 2002094848        A1    20021128    WO 2002-US15963        20020520 <--
         W:  AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,
             CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH,
             GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR,
             LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH,
             PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ,
             UA, UG, US, UZ, VN, YU, ZA, ZM, ZW
         RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH,
             CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR,
             BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG
     WO 2001046473        A1    20010628    WO 2000-US34688        20001220 <--
         W:  AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,
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CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR,
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YU, ZA, ZW
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BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

AU 2002257301 A1 20021203 AU 2002-257301 20020520 <--
US 20060183676 A1 20060817 US 2003-478268 20031118 <--
PRAI WO 2000-US34688 A2 20001220 <--
US 2001-292096P P 20010518 <--
US 1999-171929P P 19991222 <--
WO 2002-US15963 W 20020520 <--
RE.CNT 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L13 ANSWER 2 OF 10 HCAPLUS COPYRIGHT 2009 ACS on STN
TI Production of avirulent mutants of Mycobacterium bovis with vaccine properties by the use of illegitimate recombination and screening of stationary-phase cultures
AB A better tuberculosis vaccine is urgently required to control the continuing epidemic. Mol. techniques are now available to produce a better live vaccine than BCG by producing avirulent strains of the Mycobacterium tuberculosis complex with known gene deletions. In this study, 1000 illegitimate recombinants of Mycobacterium bovis were produced by illegitimate recombination with fragments of mycobacterial DNA containing a kanamycin resistance gene. Eight recombinant strains were selected on the basis of their inability to grow when stationary-phase cultures were inoculated into minimal medium. Five of these recombinants were found to be avirulent when inoculated into guinea pigs. Two of the avirulent recombinants produced vaccine efficacy comparable to BCG against an aerosol challenge in guinea pigs with M. bovis. One of these recombinants had an inactivated glnA2 gene encoding a putative glutamine synthetase.
Transcriptional anal. showed that inactivation of glnA2 did not affect expression of the downstream glnE gene. The other recombinant had a block of 12 genes deleted, including the sigma factor gene sigG. Two avirulent recombinants with an inactivated pckA gene, encoding phosphoenolpyruvate carboxykinase which catalyzes the first step of gluconeogenesis, induced poor protection against tuberculosis. It is clear that live avirulent strains of the M. tuberculosis complex vary widely in their ability as vaccines to protect against tuberculosis. Improved models may be required to more clearly determine the difference in protective effect between BCG and potential new tuberculosis vaccines.
AN 2002:818554 HCAPLUS <<LOGINID::20090630>>
DN 139:31419
TI Production of avirulent mutants of Mycobacterium bovis with vaccine properties by the use of illegitimate recombination and screening of stationary-phase cultures
AU Collins, D. M.; Wilson, T.; Campbell, S.; Buddle, B. M.; Wards, B. J.; Hotter, G.; de Lisle, G. W.
CS AgResearch, Wallaceville Animal Research Centre, Upper Hutt, N. Z.
SO Microbiology (Reading, United Kingdom) (2002), 148(10), 3019-3027
CODEN: MROBEO; ISSN: 1350-0872
PB Society for General Microbiology
DT Journal
LA English
RE.CNT 39 THERE ARE 39 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L13 ANSWER 3 OF 10 HCAPLUS COPYRIGHT 2009 ACS on STN
TI Materials and methods to modulate ligand binding/enzymic activity of α/β proteins containing an allosteric regulatory site
AB Methods of modulating binding between an α/β protein and a binding partner are provided, along with methods of identifying modulators and their use. The methods comprise contacting the α/β protein with an allosteric effector mol. which binds to an allosteric site of the α/β protein and alters the conformation of the α/β protein such that the binding of the α/β protein to a binding partner is modulated. Thus, a primary screen for inhibitors of the classical pathway complement protein C2 and alternative pathway complement protein factor B involving modifications of standard hemolytic CH50 and AH50 assays in a microtiter plate format was carried out. Lead compds. identified in this screen were submitted to a second screening using purified complement proteins to determine which stage of complement activation the compds. inhibited. Five diaryl sulfides were identified. Numerous other assays, e.g., to identify inhibitors of integrin αEβy interaction with E cadherin, inhibitors of Rac1 GDP-GTP exchange, or antagonists of E. coli 6-hydroxymethyl-7,8-dihydropterin pyrophosphokinase, were conducted as well.
AN 2002:293978 HCAPLUS <<LOGINID::20090630>>
DN 136:337341
TI Materials and methods to modulate ligand binding/enzymic activity of α/β proteins containing an allosteric regulatory site
IN Stauton, Donald E.
PA Icos Corporation, USA
SO PCT Int. Appl., 163 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2002031511	A2	20020418	WO 2001-US32047	20011012 <--
	WO 2002031511	A3	20030313		
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW				
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	CA 2425581	A1	20020418	CA 2001-2425581	20011012 <--
	AU 2002013196	A	20020422	AU 2002-13196	20011012 <--
	US 20030088061	A1	20030508	US 2001-976935	20011012 <--
	EP 1325341	A2	20030709	EP 2001-981560	20011012 <--
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
	JP 2004511496	T	20040415	JP 2002-534845	20011012 <--
	MX 2003003207	A	20040326	MX 2003-3207	20030411 <--
PRAI	US 2000-239750P	P	20001012 <--		
	WO 2001-US32047	W	20011012 <--		

L13 ANSWER 4 OF 10 HCAPLUS COPYRIGHT 2009 ACS on STN
TI Crystal structures of glutamine synthetase from Mycobacterium tuberculosis & Salmonella typhimurium: illumination of enzymatic inhibition, reaction mechanism, and regulation
AB Unavailable

AN 2001:852652 HCAPLUS <<LOGINID::20090630>>
DN 136:365688
TI Crystal structures of glutamine synthetase from
    Mycobacterium tuberculosis & Salmonella typhimurium: illumination
    of enzymatic inhibition, reaction mechanism, and regulation
AU Gill, Harindarpal Singh
CS Univ. of California, Los Angeles, CA, USA
SO (2001) 158 pp. Avail.: UMI, Order No. DA9998978
    From: Diss. Abstr. Int., B 2001, 61(12), 6299
DT Dissertation
LA English

L13 ANSWER 5 OF 10 HCAPLUS COPYRIGHT 2009 ACS on STN
TI Treatment of Mycobacterium tuberculosis with antisense
    polynucleotides
AB Methods of inhibiting the proliferation of Mycobacterium
    tuberculosis comprising contacting Mycobacterium tuberculosis
    with an effective amount of a polynucleotide complementary to an mRNA
    transcript expressed by Mycobacterium tuberculosis are provided.
    Typical methods of the invention utilize phosphorothioate modified
    antisense polynucleotides (PS-ODNs) against the mRNA of M. tuberculosis
    genes such as glutamine synthetase, aroA, ask, groES,
    and the genes of the Antigen 85 complex.
AN 2001:472980 HCAPLUS <<LOGINID::20090630>>
DN 135:73948
TI Treatment of Mycobacterium tuberculosis with antisense
    polynucleotides
IN Zamecnik, Paul C.; Horwitz, Marcus A.; Harth, Gunter
PA The Regents of the University of California, USA
SO PCT Int. Appl., 80 pp.
    CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 2

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2001046473	A1	20010628	WO 2000-US34688	20001220 <--
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW				
	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
	AU 2001024446	A	20010703	AU 2001-24446	20001220 <--
	WO 2002094848	A1	20021128	WO 2002-US15963	20020520 <--
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW				
	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
	US 20040033972	A1	20040219	US 2002-168244	20020829 <--
PRAI	US 1999-171929P	P	19991222 <--		
	WO 2000-US34688	W	20001220 <--		
	US 2001-292096P	P	20010518 <--		

RE.CNT 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L13 ANSWER 6 OF 10 HCAPLUS COPYRIGHT 2009 ACS on STN
TI Treatment of Mycobacterium tuberculosis with antisense oligonucleotides to glutamine synthetase mRNA inhibits glutamine synthetase activity, formation of the poly-L-glutamate/glutamine cell wall structure, and bacterial replication
AB New antibiotics to combat the emerging pandemic of drug-resistant strains of Mycobacterium tuberculosis are urgently needed. We have investigated the effects on M. tuberculosis of phosphorothioate-modified antisense oligodeoxyribonucleotides (PS-ODNs) against the mRNA of glutamine synthetase, an enzyme whose export is associated with pathogenicity and with the formation of a poly-L-glutamate/glutamine cell wall structure. Treatment of virulent M. tuberculosis with 10 μM antisense PS-ODNs reduced glutamine synthetase activity and expression by 25-50% depending on whether one, two, or three different PS-ODNs were used and the PS-ODNs' specific target sites on the mRNA. Treatment with PS-ODNs of a recombinant strain of Mycobacterium smegmatis expressing M. tuberculosis glutamine synthetase selectively inhibited the recombinant enzyme but not the endogenous enzyme for which the mRNA transcript was mismatched by 2-4 nt. Treatment of M. tuberculosis with the antisense PS-ODNs also reduced the amount of poly-L-glutamate/glutamine in the cell wall by 24%. Finally, treatment with antisense PS-ODNs reduced M. tuberculosis growth by 0.7 logs (1 PS-ODN) to 1.25 logs (3 PS-ODNs) but had no effect on the growth of M. smegmatis, which does not export glutamine synthetase nor possess the poly-L-glutamate/glutamine (P-L-glx) cell wall structure. The expts. indicate that the antisense PS-ODNs enter the cytoplasm of M. tuberculosis and bind to their cognate targets. Although more potent ODN technol. is needed, this study demonstrates the feasibility of using antisense ODNs in the antibiotic armamentarium against M. tuberculosis.
AN 2000:38532 HCAPLUS <<LOGINID::20090630>>
DN 132:219405
TI Treatment of Mycobacterium tuberculosis with antisense oligonucleotides to glutamine synthetase mRNA inhibits glutamine synthetase activity, formation of the poly-L-glutamate/glutamine cell wall structure, and bacterial replication
AU Harth, Gunter; Zamecnik, Paul C.; Tang, Jin-Yan; Tabatadze, David; Horwitz, Marcus A.
CS Division of Infectious Diseases, Department of Medicine, 37-121 CHS, School of Medicine, University of California, Los Angeles, CA, 90095, USA
SO Proceedings of the National Academy of Sciences of the United States of America (2000), 97(1), 418-423
CODEN: PNASA6; ISSN: 0027-8424
PB National Academy of Sciences
DT Journal
LA English
RE.CNT 25 THERE ARE 25 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L13 ANSWER 7 OF 10 HCAPLUS COPYRIGHT 2009 ACS on STN
TI Cloning and characterization of the genes encoding a cytochrome P450 (PipA) involved in piperidine and pyrrolidine utilization and its regulatory protein (PipR) in Mycobacterium smegmatis mc2155
AB Transposon mutagenesis of Mycobacterium smegmatis mc2155 enabled the isolation of a mutant strain (called LGM1) altered in the regulation of piperidine and pyrrolidine utilization. The complete nucleotide sequence of the gene inactivated in mutant LGM1 was determined from the wild-type strain. This gene (pipR) encoded a member of the GntR

family of bacterial regulatory proteins. An insertion element (IS1096), previously described for M. smegmatis, was detected downstream of the gene pipR. Three addnl. open reading frames were found downstream of IS1096. The first open reading frame (pipA) appeared to encode a protein identified as a cytochrome P 450 enzyme. This gene is the first member of a new family, CYP151. By a gene replacement experiment, it was demonstrated that the cytochrome P 450 pipA gene is required for piperidine and pyrrolidine utilization in M. smegmatis mc2155. Genes homologous to pipA were detected by hybridization in several, previously isolated, morpholine-degrading mycobacterial strains. A gene encoding a putative [3Fe-4S] ferredoxin (orf1) and a truncated gene encoding a putative glutamine synthetase (orf2') were found downstream of pipA.

AN 1999:368885 HCAPLUS <<LOGINID::20090630>>
DN 131:154332
TI Cloning and characterization of the genes encoding a cytochrome P450 (PipA) involved in piperidine and pyrrolidine utilization and its regulatory protein (PipR) in Mycobacterium smegmatis mc2155
AU Poupin, Pascal; Ducrocq, Veronique; Hallier-Soulier, Sylvie; Truffaut, Nicole
CS Laboratoire de Genetique Microbienne, Universite de Technologie de Compiegne, Centre de Recherches, Compiegne, 60205, Fr.
SO Journal of Bacteriology (1999), 181(11), 3419-3426
CODEN: JOBAAY; ISSN: 0021-9193
PB American Society for Microbiology
DT Journal
LA English
RE.CNT 54 THERE ARE 54 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L13 ANSWER 8 OF 10 HCAPLUS COPYRIGHT 2009 ACS on STN
TI An inhibitor of exported Mycobacterium tuberculosis glutamine synthetase selectively blocks the growth of pathogenic mycobacteria in axenic culture and in human monocytes: extracellular proteins as potential novel drug targets
AB Mycobacterium tuberculosis and other pathogenic mycobacteria export abundant quantities of proteins into their extracellular milieu when growing either axenically or within phagosomes of host cells. One major extracellular protein, the enzyme glutamine synthetase, is of particular interest because of its link to pathogenicity. Pathogenic mycobacteria, but not nonpathogenic mycobacteria, export large amts. of this protein. Interestingly, export of the enzyme is associated with the presence of a poly-L-glutamate/glutamine structure in the mycobacterial cell wall. In this study, we investigated the influence of glutamine synthetase inhibitors on the growth of pathogenic and nonpathogenic mycobacteria and on the poly-L-glutamate/glutamine cell wall structure. The inhibitor L-methionine-S-sulfoximine rapidly inactivated purified M. tuberculosis glutamine synthetase, which was 100-fold more sensitive to this inhibitor than a representative mammalian glutamine synthetase. Added to cultures of pathogenic mycobacteria, L-methionine-S-sulfoximine rapidly inhibited extracellular glutamine synthetase in a concentration-dependent manner but had only a minimal effect on cellular glutamine synthetase, a finding consistent with failure of the drug to cross the mycobacterial cell wall. Remarkably, the inhibitor selectively blocked the growth of pathogenic mycobacteria, all of which release glutamine synthetase extracellularly, but had no effect on nonpathogenic mycobacteria or nonmycobacterial microorganisms, none of which release glutamine synthetase extracellularly. The inhibitor was also bacteriostatic

for M. tuberculosis in human mononuclear phagocytes (THP-1 cells), the pathogen's primary host cells. Paralleling and perhaps underlying its bacteriostatic effect, the inhibitor markedly reduced the amount of poly-L-glutamate/glutamine cell wall structure in M. tuberculosis. Although it is possible that glutamine synthetase inhibitors interact with addnl. extracellular proteins or structures, our findings support the concept that extracellular proteins of M. tuberculosis and other pathogenic mycobacteria are worthy targets for new antibiotics. Such proteins constitute readily accessible targets of these relatively impermeable organisms, which are rapidly developing resistance to conventional antibiotics.

AN 1999:295798 HCAPLUS <<LOGINID::20090630>>
DN 131:82606
TI An inhibitor of exported Mycobacterium tuberculosis glutamine synthetase selectively blocks the growth of pathogenic mycobacteria in axenic culture and in human monocytes: extracellular proteins as potential novel drug targets
AU Harth, Gunter; Horwitz, Marcus A.
CS Department of Medicine, University of California at Los Angeles School of Medicine, Los Angeles, CA, 90095, USA
SO Journal of Experimental Medicine (1999), 189(9), 1425-1435
CODEN: JEMEAV; ISSN: 0022-1007
PB Rockefeller University Press
DT Journal
LA English
RE.CNT 21 THERE ARE 21 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L13 ANSWER 9 OF 10 HCAPLUS COPYRIGHT 2009 ACS on STN
TI Physical and chemical characterization of glutamine synthetase purified from Mycobacterium phlei
AB Glutamine synthetase (EC 6.3.1.2) was purified from a Gram-pos., acid-fast bacterium, M. phlei, by simple procedures with 57% recovery. The enzyme resembled that from M. smegmatis in the subunit size (56,000), mol. weight (670,000), amino acid composition, the amino acid sequence of the N-terminal, and the secondary structure. The enzyme activity was regulated by adenylylation of each subunit in the dodecameric mol. M. phlei glutamine synthetase possesses 2 useful characteristics: high thermostability and resistance to protease digestion. The enzyme was not inactivated on exposure to 60° for 2 h or 37° for 72 h, or after incubation with 1% trypsin or chymotrypsin at 37° for 12 h, pH 7.8. With saturating substrate levels, the Arrhenius plot was nonlinear and concave downward with an intersection point at 45°, and the activation energies were 3.2 and 9.6 cal/mol from the slopes. The specific activity of the highly adenylylated enzyme (E10.7) was remarkably lower than that of the slightly adenylylated enzyme (E2.5); however, both enzymes show similar profiles of the Arrhenius plot. Thus, the adenylylation of the enzyme does not affect its activation energies.
AN 1989:208260 HCAPLUS <<LOGINID::20090630>>
DN 110:208260
OREF 110:34475a,34478a
TI Physical and chemical characterization of glutamine synthetase purified from Mycobacterium phlei
AU Kimura, Kinuko; Suzuki, Hazumi; Nakano, Yoshio
CS Coll. Sci., Rikkyo (St. Paul's) Univ., Tokyo, 171, Japan
SO Journal of Biochemistry (1989), 105(4), 648-52
CODEN: JOBIAO; ISSN: 0021-924X
DT Journal
LA English

L13 ANSWER 10 OF 10 HCAPLUS COPYRIGHT 2009 ACS on STN
TI Glutamine synthetase from Mycobacterium avium
AB M. avium Was previously shown to be dependent upon NH3 or glutamine as a N source. In an effort to assess the physiol. of NH3 assimilation by M. avium, a characterization of its glutamine synthetase was performed. The enzyme from M. avium was purified by streptomycin sulfate treatment, (NH4)2SO4 precipitation, and affinity chromatog. The enzyme was unusual in that it had a pH optimum of 6.4 and maximum enzyme activity was obtained at 50-60°. The glutamine synthetase activity from batch-cultured cells decreased with increasing concentration of NH4Cl in the range of 0.25-5 μmol/mL of medium, which demonstrated a response to environmental supply of a N source. The mycobacterial enzyme was similar to the other bacterial glutamine synthetases in terms of mol. weight and sedimentation coefficient, which were 600,000 and 19.5 S, resp., and enzyme activity was lost by treatment with a glutamate analog, methionine sulfoximine. The isoelec. point was, however, pH 4.5. Treatment of the enzyme with snake venom phosphodiesterase resulted in an increase in specific activity. AMP was released by the phosphodiesterase treatment, thus demonstrating that M. avium glutamine synthetase was regulated by adenylylation modification.
AN 1984:171294 HCAPLUS <<LOGINID::20090630>>
DN 100:171294
OREF 100:25997a,26000a
TI Glutamine synthetase from Mycobacterium avium
AU Alvarez, Maria E.; McCarthy, C. M.
CS Biol. Dep., New Mexico State Univ., Las Cruces, NM, 88003, USA
SO Canadian Journal of Microbiology (1984), 30(3), 353-9
CODEN: CJMIAZ; ISSN: 0008-4166
DT Journal
LA English